Bisphosphonates as a Countermeasure to Space Flight Induced Bone Loss: SMO-021

Completed Technology Project (2006 - 2017)

Project Introduction

The purpose of this Supplementary Medical Objective is to determine whether bisphosphonates, in conjunction with the routine in-flight exercise program, will protect International Space Station (ISS) crewmembers from the regional decreases in bone mineral density documented on previous ISS flights. Two dosing regimens will be tested: (1) an oral dose of 70 mg alendronate taken weekly during flight and (2) and I.V. dose of zoledronic acid 4 mg, administered just once approximately 45 days before flight. Our rationale for including both alendronate and zoledronic acid is that two dosing options will: maximize crew participation, increase the countermeasure options available to flight surgeons, increase scientific opportunities, and minimize the effects of operational and logistical constraints. Use of both oral and I.V. options can accommodate both crew and flight surgeon preferences (e.g., based on individual drug sensitivity, relevant health conditions, or other considerations). Operational and logistical constraints may favor one option versus the other. For example, stowage limits may limit use of alendronate on certain flights, while the ability to titrate the in-flight dose in response to on-orbit measurements of bone resorption would favor the weekly dosing regimen. Long-duration (e.g., 2+ year) missions would require in-flight re-dosing of I.V. zoledronic acid. The purpose of this study is not to test one dosing option versus the other. Rather, we intend to show that bisphosphonates-plus-exercise will have a measurable effect versus exercise alone in preventing space flight induced bone loss. Secondary goals will be to document the return to normal bone remodeling post-flight in crewmembers who took bisphosphonates. See also

http://www.nasa.gov/mission_pages/station/research/experiments/239.html

Anticipated Benefits

While the primary purpose of this research is to develop a countermeasure to protect crewmembers against bone loss during long duration space flight, this research may provide insight into the mechanisms and prevention of bone atrophy in other disuse conditions.

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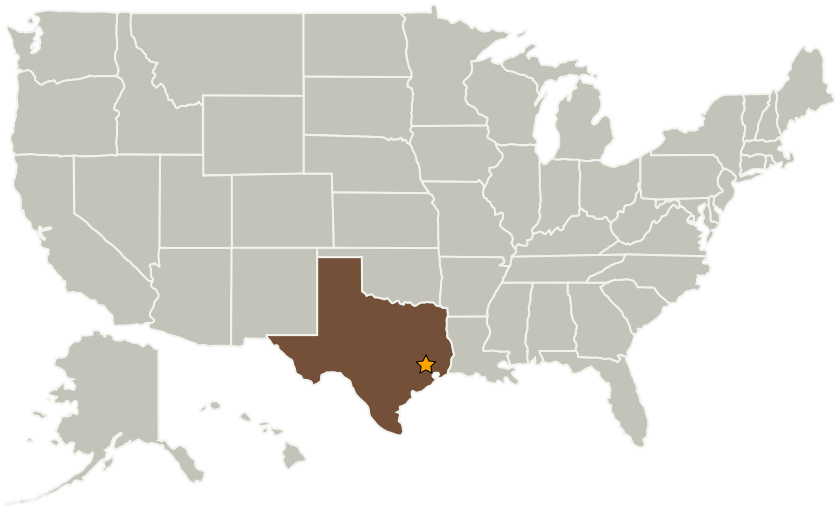
Primary U.S. Work Locations and Key Partners



Organizations Performing Work	Role	Type	Location
★Johnson Space Center(JSC)	Lead Organization	NASA Center	Houston, Texas
Universities Space Research Association(USRA)	Supporting Organization	R&D Center	Huntsville, Alabama

Primary U.S. Work Locations
Texas

Project Transitions

October 2006: Project Start

Organizational Responsibility

Responsible Mission Directorate:

Space Operations Mission Directorate (SOMD)

Lead Center / Facility:

Johnson Space Center (JSC)

Responsible Program:

Human Spaceflight Capabilities

Project Management

Program Director:

David K Baumann

Project Manager:

Jacilyn S Maher

Principal Investigator:

Adrian Leblanc

Co-Investigators:

Atsushi Okada
Harlan J Evans
Tom Lang
Takahura Yasui
Scott A Smith
Toshio Matsumoto
Jeffrey A Jones
Joyce Keyak
Toshitaka Nakamura
Hiroshi Ohshima
Kenjiro Kohri
Jean D Sibonga
Jay Shapiro
Elisabeth R Spector
Linda C Shackelford

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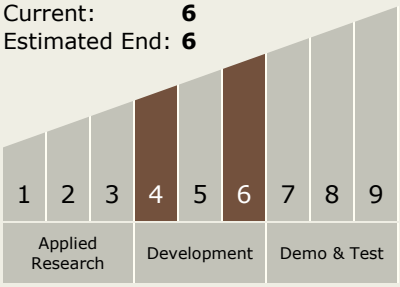
March 2017: Closed out

Closeout Summary: The original intent of this study was to test 10 long-duration crewmembers taking one of two bisphosphonate regimens: either 70 mg per week alendronate or a single infusion of 4 mg of Zoledronic acid. After the study began testing in 2009, the Johnson Space Center (JSC) Committee for the Protection of Human Subjects (CPHS) determined that only alendronate would be offered to U.S. crewmembers, while both dosing options could be offered to International Partners. It was further stipulated that only 10 alendronate subjects would be allowed. Of these, 2 dropped out prior to flight for various reasons and one crewmember reported GI symptoms very early inflight and therefore the investigators terminated the inflight dosing of this subject. We have now completed testing on the remainder 7 crewmembers taking alendronate during flight. All scheduled testing sessions for the 7 treated subjects—pre-flight, in-flight and post-flight--have been completed. DXA, pQCT, QCT, and blood and urine data have been collated and analyses of the major parameters of interest have been performed through R+30, including statistical analyses. These results were published in June 2013 in the journal Osteoporosis International (LeBlanc A, Matsumoto T, Jones J, Shapiro J, Lang T, Shackelford L, Smith SM, Evans H, Spector E, Ploutz-Snyder R, et al. (2013). Bisphosphonates as a supplement to exercise to protect bone during long-duration space flight. Osteoporosis International 24(7): 2105-2114). The results of R+12-month testing (DXA and QCT) on this group were presented at the 2014 Meeting of the American Society for Bone and Mineral Research in Houston, TX, (September 2014) and at the NASA Human Research Program Investigators' Workshop in Galveston, TX, (February 2015). Additional updates were presented at the 2016 NASA Human Research Program Investigator's Workshop in Galveston, TX, (February 2016) and the 2017 NASA Human Research Program Investigator's Workshop in Galveston, TX, in January 2017. In 2011, the study obtained approval to add a new control group, consisting of approximately 10 ISS crewmembers not taking bisphosphonates, but otherwise participating in essentially the same pre-, in-, and post-flight testing as the 7 treated subjects. The new control group should allow us to distinguish the relative effects of bisphosphonates vs. the confounder of Advanced Resistive Exercise Device (ARED) exercise, particularly at the level of trabecular vs. cortical bone. All treated subjects in this study have used the ARED device, whereas our previous control group used the older IRED or other resistive exercise device, capable of much lower loads than ARED. Testing on this new control group began in 2012, and, to date, 10 crewmembers have consented to participate. Of these, 9 crewmembers have returned from ISS flights. Eight of these have completed all post-flight testing through R+1 year, one has completed all post flight testing except one year return, and the remaining test subject has completed preflight testing. Immediate post-flight testing on this subject is expected in late 2016. It is anticipated that the control group will complete testing in ~late 2017. Preliminary results (DXA and QCT) for the first 9 of these control subjects will be presented at the 2016 Meeting of the American Society for Bone and Mineral Research in Atlanta GA, (September 2016). All testing to date for the first 8 control subjects, including QCT, DXA, pQCT, abdominal ultrasound, and blood and urine testing, has been completed on schedule and without incident. ISS sample return is complete for the first 6 control subjects. In Summary (as of March 2017) Exercise + Alendronate 7 crewmembers completed ISS mission (mean 5.5mo). All crewmembers took 70mg/wk oral alendronate starting 3 weeks prior to and during flight. Results are: reduced bone loss, eliminated elevated resorption and uncoupling, reduced urinary Ca and calculated bone strength was maintained. Results published in 2013 ARED exercise alone Ten subjects completed flight using newer exercise protocol and d

Technology Maturity (TRL)

Start: **4**
Current: **6**
Estimated End: **6**



Technology Areas

Primary:

- TX06 Human Health, Life Support, and Habitation Systems
  - TX06.3 Human Health and Performance
    - TX06.3.6 Long Duration Health

Target Destinations

The Moon, Mars

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Stories

Abstracts for Journals and Proceedings
(https://techport.nasa.gov/file/57128)

Abstracts for Journals and Proceedings
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Books/Book Chapters
(https://techport.nasa.gov/file/57133)

Project Website:

https://taskbook.nasaprs.com